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Human Plasma Metabolites Associated with Established AMD Risk Genes

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I have no financial disclosures or conflicts of interest related to the content of this presentation

Summary

- AMD risk SNPs have an impact on the plasma metabolome
- Genetic-metabolomic associations can provide unique insights into the pathogenesis of AMD

- Highest number of associations were seen with ***LIPC*** **polymorphisms**, which were associated with **glycerophospholipid metabolites**
- ***LIPC*** **gene and glycerophospholipids pathway are likely crucial in AMD pathogenesis** and may represent potential targets for treatment of AMD

AMD

Environmental
risk factors

Genetic
risk factors

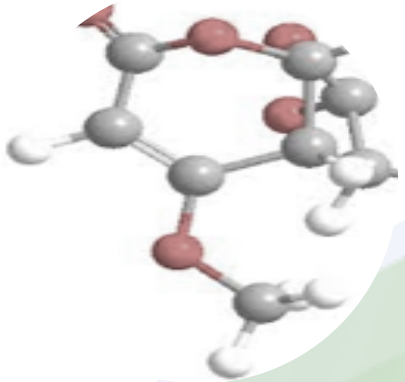
Functional consequences?

34 loci

>7,000 SNPs
(single nucleotide polymorphisms)

Fritsche LG et al. Nat Genet. 2016..

AMD

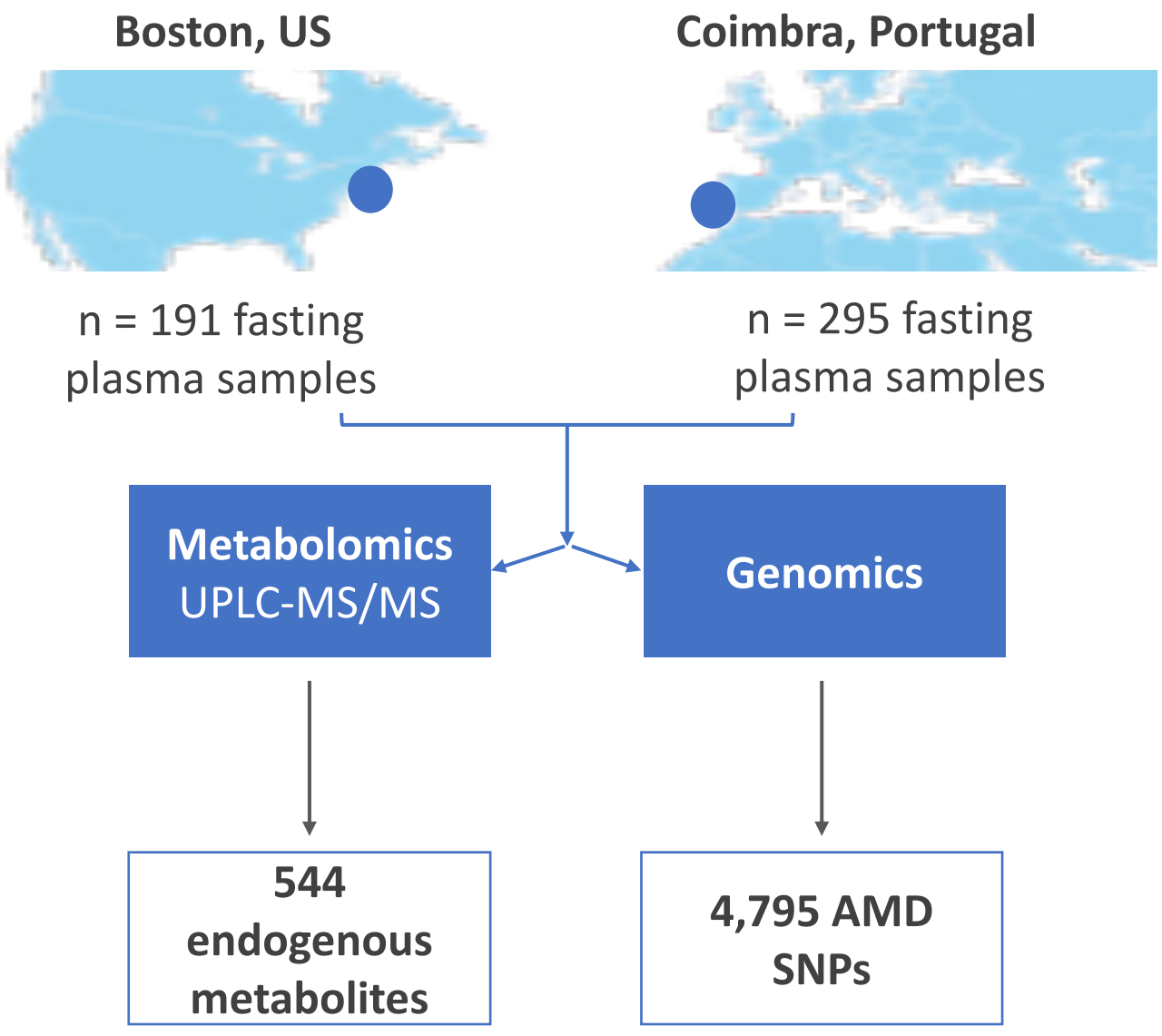


Genetic **Metabolites**

Goal

To analyze **associations between known AMD risk SNPs and plasma metabolites** in a cohort of AMD patients and controls

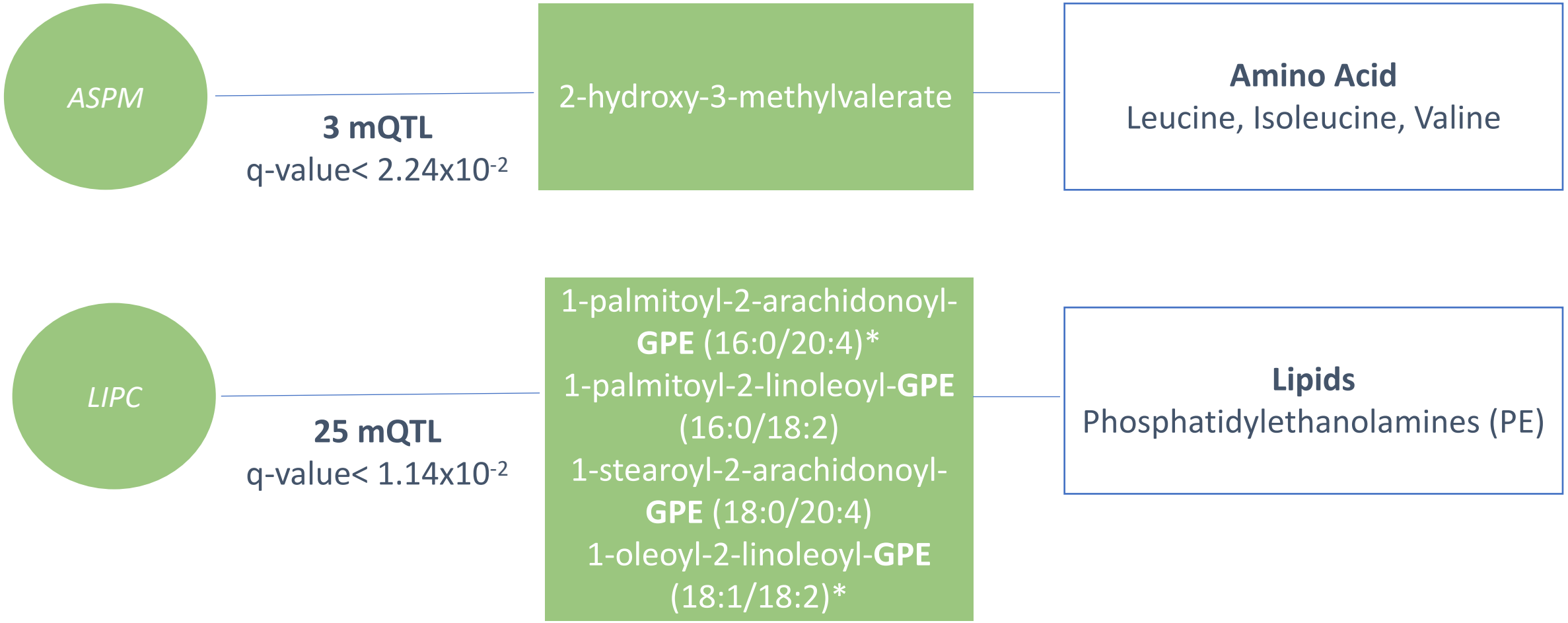
Methods


Boston, US
Coimbra, Portugal
n = 191 fasting plasma samples
n = 295 fasting plasma samples
Metabolomics
UPLC-MS/MS
Genomics
544 endogenous metabolites
4,795 AMD SNPs

Methods

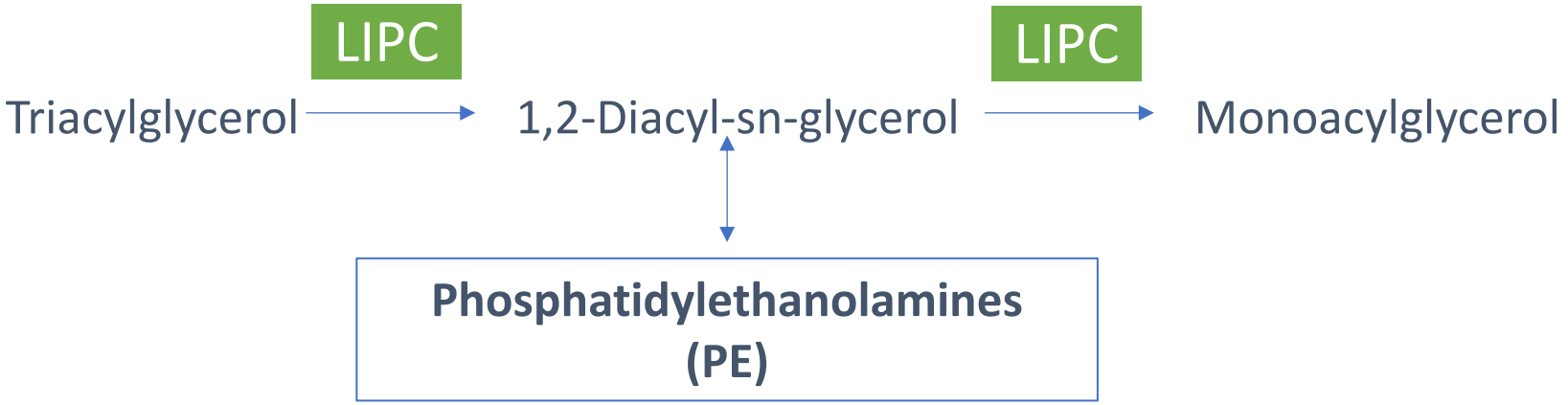
- Association between known AMD SNPs and plasma metabolites
  - Linear regression models adjusted for age, sex, smoking, 10 metabolite principal components (PCs) and 10 SNP PCs and accounting for false discovery rate
  - First for each cohort and then combined by meta-analysis

Results


ASPM
3 mQTL
q-value< 2.24x10-2
2-hydroxy-3-methylvalerate
Amino Acid
Leucine, Isoleucine, Valine
LIPC
25 mQTL
q-value< 1.14x10-2
1-palmitoyl-2-arachidonoyl-GPE (16:0/20:4)*
1-palmitoyl-2-linoleoyl-GPE (16:0/18:2)
1-stearoyl-2-arachidonoyl-GPE (18:0/20:4)
1-oleoyl-2-linoleoyl-GPE (18:1/18:2)*
Lipids
Phosphatidylethanolamines (PE)

Discussion

- *LIPC* gene with highest number of highly significant mQTL



Gieger C et al. PLoS Genet. 2008.

Limitations

- Relatively small sample size
- Cross-sectional design

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- ***LIPC*** **gene and glycerophospholipids pathway are likely crucial in AMD pathogenesis** and may represent potential targets for treatment of AMD

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Thank you!

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